SOME OBSERVATIONS ON A CASE OF SLEEPING SICKNESS: COAGULATION TIME OF BLOOD, ALBUMOSES, CHOLINE, CEREBRAL SECTIONS

BY

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(*Received for publication* 28 *October*, 1910)

INTRODUCTORY REMARKS

The observations recorded in this paper, though somewhat incomplete, are not without interest. They were made on a case of sleeping sickness in Professor Ross's clinic at the Royal Southern Hospital, Liverpool. This work was done in conjunction with other researches on the same case.*

Patient, W. A., male, age 26, was infected by the parasite of sleeping sickness in September, 1909, while he was in North East Rhodesia. Trypanosomes were observed in his peripheral blood in Africa on November 17, 1909. He died of lung and pleural complications (pneumonia and empyema) on June 29, 1910. The exact period of disease may be approximately calculated to be 300 days or thereabouts. The somnolent stage was not well pronounced. The parasite found in his blood showed a peculiar morphological feature in that some of the stout forms possessed a posterior nucleus, and has been named *T. rhodesiense* by Stephens and Fantham.† This parasite was of a marked virulence in the laboratory animals. Such in brief is the history and peculiarities of the case.

* Ross and Thomson. Proc. Roy. Soc., 82 B, pp. 411-415.

† Stephens and Fantham. Proc. Roy. Soc., 83 B, pp. 28-33 (1910).

I. *Coagulation time of blood, by Wright's method at* 37°C. (*blood heat*).

In order to understand the relations between the coagulation, leucocytes, haemoglobin and the parasites, the observations are tabulated below. They were made within the last fortnight of the patient's illness.

	Normal (Man)	June 14	June 16	June 21	June 29
Coagulation time ...	3 to 6 minutes (4 mins. 30 secs. average)	12′ 0″	5′ 25″	5′ 0″	Died
Leucocytes per mm.^{3}	10,000	25,000	4,500	3,200	
Haemoglobin index (Sahli's scale) ...	100 %	50 %	70 %	50 %	
* Parasites per mm.^{3}	—	38	32	56	

The observations are too few to lead to any definite conclusions, but one gets a general impression that the coagulation time is passing from the negative to the positive phase as the leucocytosis is passing towards leucopenia. The number of the parasites and the nature of the haemoglobin index are subject to very little variation.

II. *Absence of trypanosomes from the cerebrospinal fluid and blood.*

Patient died June 29th at about 5 p.m. Post-mortem made June 30th at about 11 a.m.

(1) The cerebrospinal fluid was carefully collected in sterilized tubes. It was mixed with a trace of blood and lymph (oedema of the brain).

(2) Tubes were centrifugalised for fifteen minutes, the supernatant fluid was pipetted off, smears were made, both from the deposits and supernatant fluid, fixed in alcohol, stained according to the Romanowsky method. The result was negative.

(3) Smears were made from the blood, fixed in alcohol stained with Romanowsky. Result, negative.

* Counted by Dr. David Thomson.

III. *Presence of albumoses in the cerebrospinal fluid.*

(1) Acetic acid and saturated sodium chloride reactions—positive.*

(2) Biuret reaction—positive.

Besides it appeared from the methodical application of other tests that the albumose belonged to the class of primary proteose.

IV. *The blood was examined for the presence of albumoses. The result was negative.*

V. *Absence of albumoses in the urine.*

The urine during life was examined for albumose. The reaction was negative; later on, in the preserved specimen of urine albumose was again found to be absent.

Patient had a large collection of pus in the pleural cavity, consequently the possibility that the albumose was due to empyema was thus eliminated by the result of the blood and urine examinations.

So that although the cerebrospinal fluid was tinged with blood, the process of exclusion leads to the conclusion that albumose was present in the cerebrospinal fluid only. According to Byrom Bramwell† the presence of albumins, together with lymphocytosis in the cerebrospinal fluid, are supposed to be of early diagnostic value in the incipient stage of parasyphilitic lesions like tabes and general paralysis of the insane. The exact origin of albumose is doubtful; either it may be due to chronic meningo-encephalitis or to toxic products of protozoa or bacteria. Whatever the cause may be it is evident that the presence of albumose is not restricted to the parasyphilitic lesions only.

Its presence in the cerebrospinal fluid in the *incipient* stage of chronic meningo-encephalitis (*T. gambiense*) requires to be determined. But how far it may be of diagnostic value in the case of sleeping sickness is another question.

VI. *Presence of choline.*

Mott and Halliburton have shown that in general paralysis of the insane the marked degeneration that occurs in the brain is

* Boston, Clinical Diagnosis (1904), p. 216.

† Personal communication.

accompanied by passing of the products of degeneration into the cerebrospinal fluid, and of these nucleo-proteid and choline (decomposition product of lecithin) are those which can be most readily detected.

This is not peculiar to general paralysis of the insane, but choline can be detected in various other nerve degenerations.

The point of peculiar interest is that the pathological changes in general paralysis of the insane and sleeping sickness are more or less similar. The test used for choline was that of Mott and Halliburton, viz., the production of characteristic octohedral crystals of the platinum double salt from the alcoholic extracts of the cerebrospinal fluid. The result was positive.

Control tests were made with the 15 per cent. alcohol and absolute alcohol used in the original test, but these were negative.

VII. *Blood.*

With the above test it was found that choline was absent in the blood.

VIII. *Absence of choline in the blood of animals infected with the parasite of the case.*

The test applied was the modified method of Mott.* It consisted in the formation of the brownish-black rectangular plates of *choline periodide*.

The number of the trypanosomes per mm.^{3} at the time of the experiment and before death of the animals are given below.

	Trypanosomes at the time of the experiment	Trypanosomes before death
Rat 1.—Weight 182 grams	20,085 per mm.^{3}	126,000 per mm.^{3}
,, 2.—Weight 220 grams	56,320 ,,	100,400 ,,
Guinea-Pig 1.—952 grams	3,328 ,,	6,000 ,,
,, 2.—880 grams	4,416 ,,	30,720 ,,
Two control rats	0	0

* *Lancet*, July 9, 1910, p. 80.

Thus choline was absent in the blood practically at the height of the parasite infection.

According to Plimmer* the brains of rats that have been inoculated with the human trypanosomes have shown the peculiar perivascular infiltration. It is interesting to note from my observations that choline failed to enter into the blood, or in other words the products of nerve degeneration have not passed into the blood.

IX. *Effect of products of nerve degeneration in the cerebrospinal fluid (i.e., choline and nucleo-proteid) from the case of sleeping sickness—on the coagulation time of blood and the percentage of haemoglobin in the rat.*

	Before inoculation of cerebrospinal fluid intraperitoneally	After inoculation of the same intraperitoneally				
		1st day	3rd day	4th day	5th day	6th day
	min. sec. min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.
Coagulation time (By Wright's method at half blood heat)	4 25 to 4 30	3 15	7 5	6 40	6 55	10 46
Haemoglobin ... (Sahli)	120%	80%	55%	40%	60%	80%

We may not be able to draw any inferences from the smallness of this experiment, but one fact remains that the cerebrospinal fluid from the case of sleeping sickness contained a product which influenced the negative and the positive phase of coagulation, and so far as is known on the subject, it may be the nucleo-proteid.

X. *Sections of the brain tissue.*

The brain tissue was kindly lent to me by Dr. Stephens to whom my thanks are due.

The tissue was embedded in paraffin, sections were cut and stained with haematoxylin and eosin.

* Allbutt and Rolleston. System of Medicine, Vol. II, Part II, p. 215.

Microscopical appearances.

The perivascular spaces around the blood vessels in the substance of the brain were infiltrated with mononuclear leucocytes, chiefly lymphocytes. This change is typical of the sleeping sickness brain where the infection is due to *T. gambiense*. The infiltration was not enormous. I have applied a method of counting the mononuclears in the perivascular spaces. The sections cut were 8 μ in thickness.

Length of the vessel in section in μ	Breadth of the vessel in section in μ	Number of the mononuclears
100	22·8	34
68	68	48
100	68	72
100	100	56
100	100	56
68	68	45
136	68	40
100	85	45
136	100	116
100	85	35
136	100	118
100	85	95
100	85	68
100	85	55
100	85	40
100	85	40
100	85	40
136	100	150
68	68	40
100	34	50
100	34	48
Average 102	72·8	61 mononuclears

That is in a space of 102 μ × 72 μ × 8 μ there are 61 mononuclear leucocytes.

Some of the brain tissue was sent to Dr. Mott, F.R.S., by Professor Ross for his opinion. The report given by Dr. Mott appears below:—

Report on the Examination of Brain Tissue sent by Major R. Ross

Two small portions of brain embedded in paraffin were received; one was a small piece of cerebellum; the other was a small portion of white subcortical tissue, location not definable. Sections of 5μ were cut and stained by polychrome, Giemsa and Heidenhain haematoxylin methods.

All the sections examined showed a well-marked perivascular infiltration with lymphocytes and plasma cells, indistinguishable from that which I have seen in all cases of sleeping sickness. The membranes were absent in both pieces of tissue so I cannot say they were affected. Apparently there was evidence of glia hyperplasia and proliferation in the subcortical tissue. Inasmuch as subcortical and cerebellar tissues always show a more marked perivascular infiltration than the cortex in early cases it would have been more satisfactory if different regions of the cortex could have been examined. For unless the perivascular infiltration affects diffusely the cerebral cortex (seat of consciousness) one would not expect marked lethargy. From an examination of a large number of cases of sleeping sickness I have come to the conclusion that the subcortical structures are affected primarily and that there is a parallelism between the depth of the lethargy and the intensity and diffuseness of affection of the meninges and cortical vessels with neuroglia proliferation and changes in the nerve cells. A large number of the vessels show fibrin filaments indicative of a pneumonic condition.